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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/705,438	11/10/2003	John Dodgson	06275-295002	4606

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Fish & Richardson P C
ATTN: Janis K Fraser
225 Franklin Street
Boston, MA 02110-2804

EXAMINER	
BOWERS, NATHAN ANDREW	
ART UNIT	PAPER NUMBER
1744	

MAIL DATE	DELIVERY MODE
08/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/705,438	DODGSON ET AL.	
	Examiner	Art Unit	
	Nathan A. Bowers	1744	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 14-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,14,16-23,25-32,34 and 35* is/are rejected.

7)☒ Claim(s) *15,24 and 33* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *111003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1) Claims 1, 17, 28 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Chang (US 4822470).

With respect to claims 1, 17 and 32, Chang discloses an apparatus and method for introducing a substance into an object. A first microfabricated channel comprising an inlet (Figure 4:41) and outlet (Figure 4:44) is used to deliver an object in a first fluid (Figure 4:19) to a permeation region. The microfabricated channel is also used as a means to deliver a substance to the permeation region so that the substance is introduced into the object. This is disclosed in column 9, lines 32-47 and column 11, lines 26-61. A means for causing permeability (Figure 4:25) of the wall of the object is provided and includes a first and second electrode dimensioned and arranged to deliver a voltage pulse to the first fluid.

With respect to claim 28, Chang discloses the apparatus in claim 1 wherein the microfabricated channel is formed between two glass plates (Figure 4:34). Since glass is transparent, the plates allow one to optically inspect objects flowing through channel.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2) Claims 2, 14, 31, 34 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang (US 4822470).

With respect to claims 2, 14, 34 and 35, Chang discloses the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 102 rejections above. Although Chang states in column 9, lines 39-41 that the channel is approximately 500 microns in diameter, it would have been obvious to one of ordinary skill in the art to fabricate the apparatus so that the channel diameter is any size recognized to be capable of accommodating electroporation. Channel diameter is considered to be a result effective variable that is optimized through routine experimentation. At the time of the invention, it would have been apparent to fashion the channel disclosed by Chang so that it is 30 or 50 microns in width if it was determined that these measurements produce the best results. See MPEP 2144.05. Micromachining techniques suitable for creating 30-50 micron channels are well known in the art.

With respect to claim 31, Chang discloses the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 102 rejections above. Although Chang does not expressly disclose that a plurality of channels and permeation regions arranged in an array, it would have been obvious to perform multiple experiments simultaneously in parallel. Since Chang already discloses every structural feature set forth in the claimed invention, the creation of an array of channels would simply require the duplication of parts that are known in the art. Mere duplication of parts does not result in a new device that is patentable difference over the prior art.

3) Claims 16, 18-20 and 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang (US 4822470) as applied to claim 1, and further in view of Nicolau (US 5612207).

With respect to claims 16 and 18-20, Chang discloses the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 102 rejections above, however does not expressly state that pump is provided for regulating fluid flow, or that a second channel is provided for delivering the substance to the first channel.

Nicolau discloses a device for introducing biochemical compounds into cells through electroporation using a device comprising a flow cell (Figure 9:20) a two electrodes (Figure 9:202). The biochemical compounds are stored in a reservoir (Figure 1:50), are moved through a channel using a pump (Figure 1:40), and introduced to the fluid passage carrying cells at a junction point (Figure 1:67). This is apparent from column 13, line 20 to column 15, line 32 and Figure 1.

Chang and Nicolau are analogous art because they are from the same field of endeavor regarding electroporation systems.

At the time of the invention, it would have been obvious to provide the apparatus of Chang with a pump and a second channel for carrying compounds to be introduced to a cell population. The use of a pump in communication with a plurality of fluidic channels is considered to be a well known arrangement, and pumps are widely regarded as a common means by which to move a fluid through a system in a controlled manner.

With respect to claims 25-27, Chang discloses the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 102 rejection above, however does not expressly state that the apparatus is formed on a silicon substrate.

Nicolau discloses the apparatus described above. In addition, Nicolau teaches in column 20, lines 45-58 that the electroporation flow cell is constructed from silicon.

At the time of the invention, it would have been obvious to fabricate the apparatus disclosed by Chang on a silicon substrate. As evidenced by Nicolau, silicon is well known in the art as a suitable material for the formation of biological reaction chambers. Silicon is compatible with many recognized micromachining techniques, and is relatively inexpensive.

4) Claims 21-23, 25-27 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang (US 4822470) as applied to claim 1, and further in view of Beebe (US 6193647).

With respect to claims 21-23, Chang discloses the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 102 rejections above, however does not expressly state that a means is provided to restrain a cell in a desired position adjacent to the two electrodes.

Beebe discloses a microfluidic cell handling system that is used for culturing, sorting, testing and evaluating biological samples. Beebe teaches in column 4, line 30 to column 5, line 4 that means are provided to locate cells at a desired location within

the microchannel. This is clearly illustrated in Figure 2. Column 4, lines 34-38 specifically state that the cells are precisely positioned at electrodes.

Chang and Beebe are analogous art because they are from the same field of endeavor regarding microfluidic systems designed for cell testing.

At the time of the invention, it would have been obvious to incorporate the handling device disclosed by Beebe in the apparatus of Chang. Beebe teaches that it is known in the art to modify the diameter of a microfluidic channel in order to trap a specified cell at a desired location. It would have been desirable to alter the channel configuration of Chang in this manner to ensure that the cells are able to fully interact with the electrodes and encourage efficient electroporation.

With respect to claims 25-27 and 39, Chang and Beebe disclose the combination as previously described above. In addition, Beebe describes in column 3, lines 55-67 that the microchannels are formed within a silicon wafer. Additionally, Beebe teaches in column 4, lines 34-38 that photodetectors and light sources are implemented in order to evaluate the cells at target locations formed by the handling devices. Intra-red sources are well known in the art as effective light sources.

5) Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chang (US 4822470) as applied to claim 1, and further in view of Mangano (US 6589786).

Chang discloses the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 102 rejection above, however does not expressly disclose that a sorting means is arranged to separate transfected cells from non-transfected cells.

Mangano discloses a flow through electroporation flow unit (Figure 7:151) comprising two electrodes (Figure 7:152 and Figure 7:153). Column 45, line 49 to column 46, line 23 indicates that flow cytometers are provided downstream from the electroporation flow unit in order to remove undesirable cells from the sample stream.

Chang and Mangano are analogous art because they are from the same field of endeavor regarding electroporation systems.

At the time of the invention, it would have been obvious to utilize a flow cytometer downstream from the electroporation unit disclosed by Chang. Mangano indicates that cytometers are known in the art as effective means capable of separating porated cells from non-porated cells. A cytometer would therefore be useful in concentrating transfected cells for collection and further study.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6) Claims 1-35 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,653,136. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of US 6,653,136 disclose the use of a microfabricated apparatus the comprises two electrodes capable of producing an electric field to permeate the wall of a cell. The claims of US 6,653,136 indicate that the electric field is produced automatically, and is sufficient to enable the movement of foreign molecules into the cell.

Allowable Subject Matter

Claims 15, 24 and 33 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The prior art does not disclose the use of an electroporation system that is capable of applying a voltage pulse when the cell is detected to be in a desired position. Chang does not disclose the use of a sensor capable of recognizing the position of a particular cell, and therefore cannot commence poration automatically.

This indication of allowable subject matter is in agreement with the claims of U.S. Patent No. 6,653,136 which rely on this limitation for patentability.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan A. Bowers whose telephone number is (571) 272-8613. The examiner can normally be reached on Monday-Friday 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gladys Corcoran can be reached on (571) 272-1214. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/William H. Beisner/
Primary Examiner
Art Unit 1744

NAB